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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Upvan NARANG et al.

Group Art Unit: 1615

Application No.: 09/430,177

Examiner: T. WARE

Filed: October 29, 1999

Docket No.: 100448.01

For: ADHESIVE APPLICATOR TIP WITH A POLYMERIZATION INITIATOR,  
POLYMERIZATION RATE MODIFIER, AND/OR BIOACTIVE MATERIAL

DECLARATION UNDER 37 C.F.R. §1.132

Director of the U.S. Patent and Trademark Office  
Washington, D.C. 20231

Sir:

I, Upvan Narang, a citizen of the United States, hereby declare and state:

1. I have a Ph.D. degree in Analytical Chemistry, which was conferred upon me by the State University of New York in Buffalo, New York in 1995.
2. I have been employed by Closure Medical Corporation since 1997 and I have had a total of eleven years of work and research experience in biomaterials.
3. I am a co-inventor of the invention disclosed and claimed in the above-identified patent application, and I have reviewed its disclosure and claims.
4. I and/or those under my direct supervision and control have conducted the following tests:

Experiments were conducted to compare the setting time of cyanoacrylate adhesive compositions where various solvents are used as a carrier for an initiator for the cyanoacrylate.

That is, as described in the present application, it has been discovered that different setting characteristics are provided by selecting different carrier solvents for the initiator. Thus, for example, where methanol is used to apply the initiator to the applicator tip, a shorter or equivalent set time, lower set temperature, and different distribution profile are observed.

In order to further compare the setting characteristics of different solvent-initiator systems, a gel set time test was performed. The gel set time test differs from the test described in the present application in that a larger amount of adhesive material is used, and the entire test is conducted in the liquid phase. The gel set time figures obtained from the gel set time test are thus different in magnitude and trends from the set time figures described in the present application. An advantage of this gel set time test is that the number of variables affecting the outcome of the test can be substantially reduced, so that the effect of the solvent can be isolated. In contrast, the set time and set temperature testing described in the specification is more prone to a number of outside environmental influences.

The testing described herein was conducted to compare the gel set times of cyanoacrylate adhesive using benzalkonium chloride as the initiator. The initiator was provided mixed with one of three different solvents -- acetone, ethanol or methanol -- to determine how the particular solvent effects the gel set time.

5. The gel set time test was conducted as follows:

The initiator solution is prepared by weighing out 5.00 +/- 0.01 g of benzalkonium chloride and transferring it to a 1 L volumetric flask. To the flask is added the particular solvent (acetone, ethanol or methanol) in a sufficient amount to provide a 0.5 vol% solution of benzalkonium chloride. The prepared solution was stored in a refrigerator until ready for use.

A stabilized 2-octyl cyanoacrylate adhesive composition was obtained. Samples from the same cyanoacrylate adhesive composition lot were used for all of the testing described below.

A. Acetone Solvent Test Procedure

2 mL of the cyanoacrylate adhesive composition was aspirated into a 3 mL tuberculin syringe, and dispensed into a 7 mL screw cap bottle. A stirring bar was placed into the sample bottle, and the bottle was placed on a stir plate. The stir plate was set to a setting where a vortex is just formed in the sample that comes close to the stir bar.

Using a 20-200  $\mu$ L pipette set to 200  $\mu$ L, the 0.5% benzalkonium chloride/acetone solution was dispensed into the stirring sample, and a timer was started.

When the stir bar stopped, indicating that the cyanoacrylate adhesive composition gelled, the timer was stopped. This was taken as the gel set time for the composition.

The test was performed three times, and the resultant values were averaged to provide a gel set time for the composition and initiator/solvent mixture. The results are provided below in Table 1.

B. Ethanol Solvent Test Procedure

The same procedures described above were repeated, except that a solution of benzalkonium chloride in ethanol was prepared. The testing was conducted, and the results were recorded as reported in Table 1 below.

C. Methanol Solvent Test Procedure

The same procedures described above were repeated, except that a solution of benzalkonium chloride in methanol was prepared. The testing was conducted, and the results were recorded as reported in Table 1 below.

Table 1  
Gel Set Time (Minutes) for Different Solvent/Initiator Systems

Test	Ethanol (5074.7 ppm)	Methanol (5069 ppm)	Acetone (5074.7 ppm)
1	8.12	15.33	0.38
2	7.3	15.14	0.43
3	7.38	16.26	0.41
Average	7.6	15.6	0.4
Standard Dev.	0.5	0.6	0.0
Relative Standard Dev.	5.9	3.8	6.2

6. The above test data clearly indicates that the results provided by methanol are very different from the results provided by either acetone or ethanol. As described in the present application, where the initiator is applied using methanol as the solvent, desired set characteristics are provided as compared to results where the initiator is applied using acetone as the solvent.

These results are specifically contrary to the statement made in the Office Action dated March 13, 2002, where it is asserted that "[o]ne skilled in the art would expect the two compounds [methanol and ethanol] to have similar properties." See Office Action at page 3, third full paragraph. Rather than having similar properties, the above test clearly shows that the compounds in fact have very different properties, which in turn affect the set characteristics of cyanoacrylate adhesive compositions initiated using an initiator that was solvated in the particular solvent.

7. I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine and/or imprisonment under Section 1001 of Title 18 of the United

States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Date: 8/7/02

Upvan Narang  
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